EPA

MRID

NUMBER

NR00621

DOW CORNING

NR-422042-01

February 13, 1992

Office of Pesticide Programs
Document Processing Desk -- 6(a)(2)
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Dear Sir:

Re: FIFRA SECTION 6(A)(2) NOTIFICATION OF ADVERSE EFFECTS FOR AN IMPURITY PRESENT IN DOW CORNING'S ANTIMICROBIAL AGENTS

In accordance with Section 6(a)(2) of FIFRA, DOW CORNING CORPORATION is submitting the following information.

SUBMITTER AND REGISTRANT: DOW CORNING CORPORATION
2200 West Salzburg Road
Midland, Michigan 48686-0994

EPA REGISTRATION NOS: 34292-1, 34292-2, 34292-3, 34292-5. 34292-6

INFORMATION SUBMITTED: Preliminary results from a 28-day vapor inhalation toxicity study on a chemical substance that is present as an impurity in DOW CORNING's antimicrobial products.

SUBSTANCE TESTED: See CONFIDENTIAL APPENDIX A. The substance is hereafter referenced in this report as "the impurity".

PRELIMINARY RESULTS: The impurity shows the potential for genetic activity in an in vivo system. A statistically significant increase in the incidence of micronuclei in bone marrow cells was noted at the highest dose levels.

CURRENT ASSESSMENT: Based on a similar in vivo test of the substance that would more accurately represent exposure to the pesticide product (as opposed to the impurity tested here) and considering the use patterns of these materials, there is no reason to suspect the tested impurity would be present when the product is used as directed. DOW CORNING is planning further studies with the impurity.

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DISCUSSION:

In 1990 and 1991, in vitro testing conducted on the impurity by DOW CORNING indicated that the substance was genetically active and TSCA, Section 8(e), reports were filed. Additional understanding was needed, so a decision was made to conduct an in vivo test on the impurity. In an ongoing 28-day vapor inhalation study with the impurity in rats involving repeated exposure of test animals to 10, 50, 100 and 200 ppm impurity for 6 hours per day, 5 days per week, a statistically significant increase in the incidence of micronuclei in bone marrow cells was noted in female rats at 200 ppm (equivalent to a total dose of over 5000 mg/kg body weight), but not at lower doses. Accordingly, it would appear that the impurity may have some potential for genetic activity in an in vivo system.

Once the study on the impurity in an in vivo system has been completed, DOW CORNING will provide EPA with a copy of the final report. If additional studies are indicated, DOW CORNING will conduct them and notify the Agency of any pertinent preliminary findings and will submit a final report when the studies have been completed.

The impurity is present in DOW CORNING's antimicrobial products at the levels indicated in the confidential statements of formulae in CONFIDENTIAL APPENDICIES B AND C. These products are used in the treatment of a variety of textiles and hard surfaces. Treatment of the substrate is accomplished by mixing a small quantity of antimicrobial agent with water and then applying it by dipping, spraying, or other conventional means by certified commercial applicators to achieve 0.1 to 1.0% by weight active ingredients. Adding the antimicrobial agent to water induces a hydrolysis reaction which converts the methoxy functional groups on the active ingredient, and on some of the impurities, to hydroxy groups.

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In Phase 2 of reregistration, DOW CORNING was required to conduct several mutagenicity tests. These were: L5178Y Mouse Lymphoma Forward Mutation Assay (MRID #'s 41296801, 41353302, and 41353301), Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay (MRID # 41296804), an in vivo Mouse Micronucleus Assay (MRID# 41296803), and a Host Mediated Assay For Detection Of Mutations (MRID# 58118 and 40385206). With an objective to evaluate the chemical form of the material to which humans and animals might be exposed during or after treatment, a hydrolyzate of the antimicrobial agent was made. This material contains partially hydrolyzed methoxy groups as would exist during application and drying. With permission from the U.S. EPA, this form of the antimicrobial agent was used in the studies listed above. The composition of the [redacted] is described in the confidential statement of formula in CONFIDENTIAL APPENDIX D.

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2

DOW CORNING® 5700 hydrolyzate which contains the impurity, and/or the hydrolysis product of the impurity, was found not to be genetically active in the Mouse Lymphoma Forward Mutation Assay and does not induce Unscheduled DNA Synthesis. It was found not to produce a mutagenic response in S. typhimurium (strain G-46) following a host-mediated assay using albino rats. DOW CORNING® 5700 hydrolyzate was also administered to mice via oral gavage at doses of 500, 2500, and 5000 mg/kg for the Mouse Micronucleus Assay. It did not induce a significant increase in micronuclei in bone marrow polychromatic erythrocytes and was, therefore, considered negative in the in vivo Mouse Micronucleus test.

Considering the results from this study, related studies, and the use pattern of the antimicrobial agents, it is believed that these products should not pose a genetic risk to animals or humans, when used as directed.

If additional information is required please contact Michael G. Hales, Regulatory Compliance Specialist, DOW CORNING CORPORATION, at the address provided below or by telephone at 517-496-5616.

Sincerely,

Forrest A Stark

Dr. Forrest O. Stark
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Director of Health and Environmental Sciences
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